

## **REMARKS**

### **I. Support for the Amendments**

Claims 1, 24, 25, 30-33, 37, 43, 48, and 49 have been amended. No new matter has been added by virtue of these amendments.

Support for claims 1, 24, 25, 30-33, 37, 43, 48, and 49 as amended can be found in the original specification, e.g., from pages 2-5, in the Examples and in the original and amended claims. Detailed support for amended claims 1, 24, 25, 30-33, 37, 48, and 49 can be found on pages 2-4, 5, and 6-7 of the specification, particularly in the carry-over paragraph on pages 2-3 and in claim 2 (now canceled), as well as in the middle paragraph on page 5.

### **II. Status of the Claims**

Claims 1, 3-35, and 37-49 were previously pending in the present application. In the Office Action, mailed June 23, 2005, the Examiner rejected claims 1, 3-12, 15-33, 37-42, and 45-49 and has objected to claims 43 and 44. The Examiner has allowed claims 13, 14, 34 and 35.

Currently, claims 1, 3-35, and 37-49 are pending in the application, with claims 1, 13, 14, 24, 25, 30, 31, 34, 35, 37 being the independent claims.

### **III. The Information Disclosure Statement**

Applicants filed an Information Disclosure Statement concurrently with the Amendment mailed on January 26, 2005. Applicants respectfully request the Examiner to acknowledge the Information Disclosure Statement.

**IV. The Supplemental Declaration and Power of Attorney in Compliance with 37 C.F.R. 1.63(c)**

The Examiner has acknowledged papers filed under 35 U.S.C. §119 (a)-(d) on an application filed in the United Kingdom on 17 November 1998. On 17 May 2001, the present application was filed under 35 U.S.C. §371, along with a Declaration and Power of Attorney bearing the signatures of both joint inventors. The Examiner requested a supplemental oath or declaration listing this application and in compliance with 37 C.F.R. §1.63(c).

A Supplemental Declaration and Power of Attorney, which was signed by inventor Dr. Neil James Butt, was filed with the Amendment mailed January 26, 2005. Applicants have endeavored to obtain the signature of Dr. Christopher Peter Jones, but have been unable to do so.

Applicants are filing herewith a Petition under 37 C.F.R. §1.47(a) to accept the Supplemental Declaration & Power of Attorney executed by inventor Dr. Neil James Butt on behalf of him and the non-signing inventor, Dr. Christopher Peter Jones, in order to avoid prejudice to the Assignee. The Petition is accompanied by a supporting Statement of Facts Regarding Inventor's Refusal to Sign Supplemental Declaration and a Supplemental Statement by Applicants' undersigned representative.

The Examiner is invited to telephone Applicants' undersigned representative if it will assist in any way.

**V. Rejection of Claims 1, 3-12, 15-23, and 37-40 Under 35 U.S.C. §112, First Paragraph, Is Traversed, but Accommodated**

The Examiner has rejected claims 1, 3-12, 15-23, and 37-40 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner has stated that this is a new rejection. The Patent Office alleges that the claims contain subject matter, which is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In particular, the Patent Office alleges:

The limitation that "most of the plasmid DNA is isolated from the genomic DNA" has been added to the claims. Applicant has not indicated where support for this limitation is found. The examiner has been unable to find literal support in the originally filed specification for the phrase that "most of the plasmid DNA is isolated from the genomic DNA". While the specification teaches that the plasmid DNA is isolated from plasmid DNA containing material, it does not demonstrate that most of the genomic DNA is absent from the sample or that the method results in separation of most of the genomic DNA from the sample. . Therefore, the limitation of adding "" is impermissible NEW MATTER. [P. 3.]

Applicants respectfully disagree, but have amended claims 1 and 37 in order to further prosecution of this case in a more timely manner.

The Table of Extraction Mixtures Tested (pages 6-7) describes the Plasmid DNA Recovery as No, Poor, OK, or Good. "Good" is defined as "Approximately 1 µg DNA recovery"; "OK" is defined as "Approximately 200 ng DNA recovery"; and "Poor" is defined as "Just visible on agarose gel electrophoresis." Clearly, some separation conditions are better than others. Those that are "OK," for example, have only some plasmid recovery. Therefore, it appears that, while these conditions are "OK" and, therefore, may be of some use, they do not result in an absolute sequestration of the plasmid DNA in the organic (e.g., butanol) phase. Rather, it may be that a larger percentage of the plasmid DNA in these samples is remaining in the aqueous phase with the genomic DNA. An "OK" plasmid

recovery may be acceptable in some circumstances (i.e., only 20% of the amount of DNA from a “Good” recovery).

Moreover, it is well-known to those of ordinary skill in the art that the difference between plasmid DNA and genomic DNA is readily observable on an agarose gel electrophoresis, due to the generally different sizes, conformations, and charges and, therefore, migration rates of the two types of DNA. The results of an agarose gel electrophoresis, which not involve undue experimentation, would enable the practitioner of the present invention to observe whether “most of the plasmid DNA is isolated from the genomic DNA.”

Regardless, Applicants wish to make it clear on the record that the partitioning of plasmid DNA and/or genomic DNA need not be 100% in order to fall within the limitations of the present claims.

Claims 3-12, 15-23, and 38-40 are either directly or indirectly dependent on claim 1, and the same arguments apply to those claims.

For these reasons, while Applicants respectfully traverse the Examiner’s rejection of claims 1, 3-12, 15-23, and 37-40 under 35 U.S.C. § 112, first paragraph, Applicants respectfully assert that the claims are in a condition for allowance.

Therefore, Applicants request reconsideration and withdrawal of the rejections made under 35 U.S.C. §112, first paragraph.

**VI. Rejection of Claims 24-33 and 45-49 under 35 U.S.C. § 112, Second Paragraph, Is Traversed, but Accommodated**

The Examiner has rejected claims 24-33 and 45-49 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

In particular, with respect to claims 24-33 and 45-47, the Patent Office alleges:

Claims 24-33 and 45-47 recites the limitation "extraction solution " in said claims. There is insufficient antecedent basis for this limitation in the claim. An extraction solution need not be in a mixture. [P. 4.]

Applicants have amended claims 24, 25, 30, and 31 to replace "solution" with "mixture." Claims 28, 29, 32, 33, and 45-47 are either directly or indirectly dependent on claim 24, and claims 26 and 27 are either directly or indirectly dependent on claim 25.

In particular, with respect to claims 48 and 49, the Patent Office alleges:

Claims 48-49 are vague and indefinite in that the metes and bounds of the word "substantially" are unclear. The term "substantially" is a relative one not defined by the claim, no single set of conditions is recognized by the art as being "substantial" and because the specification does not provide a standard for ascertaining the requisite degree. [P. 4]

Furthermore, with respect to Applicants' previous arguments, the Patent Office alleges:

Applicants traverse the claim rejections under 35 U.S.C. 112, second paragraph on pages 10-12 of the amendment filed 1/26/05. Applicants argue that claim language is not required to be limited only to a single set of conditions but can be defined in the dictionary or described in the specification through examples and methods. The instantly recited term "substantially" is defined in the dictionary and described in example 1. In this example, separation conditions were evaluated as "OK", "Good" and "Poor". Applicants argue that even for separation conditions that do not result in absolute sequestration of the plasmid DNA in the organic phase, the methods may be of some use. Furthermore, it is argued that the differences between plasmid DNA and genomic DNA can be evaluated on agarose gels, which would enable the practitioner of the present invention to observe whether the plasmid DNA was "substantially" in one fraction and genomic DNA in the other. Finally applicants argue that the plasmid

DNA and/or genomic DNA need not be 100% in order to fall within the limitations of the claims.

Applicants' arguments filed 1/26/05 has been fully considered but they are not persuasive. The courts have determined that use of terms such as "substantial portion" are indefinite when the specification lacked some standard for measuring the degree intended *Ex parte Oetiker*, 23 USPQ2d 1641. In the instant case, the specification describes extraction mixtures that are able to generate DNA purification that is "good", 1 µg of DNA, "OK" that is 200 ng and "Poor" which is just visible DNA. However, it is unclear how these values demonstrate the relative amount of plasmid, which has been partitioned into the butanol versus aqueous phase or the separation conditions. Rather these numbers indicate the actual amount of DNA isolated from samples using the instantly recited methods. Therefore, the instant specification lacks any standard for measuring the requisite degree intended for the term "substantially". [Pp. 4-5.]

Applicants continue to traverse this rejection for reasons already outlined at length throughout the prosecution of this case (see, e.g., the Amendment mailed January 26, 2005). In the interests of furthering prosecution in a timely manner, Applicants have amended claims 48 and 49.

Regardless, Applicants wish to make it clear on the record that the partitioning of plasmid DNA and/or genomic DNA need not be 100% in order to fall within the limitations of the present claims.

For these reasons, Applicants respectfully traverse the Examiner's rejection of claims 24-33 and 45-49 under 35 U.S.C. § 112, second paragraph, and assert that claims 24-33 and 45-49 are in a condition for allowance.

Therefore, Applicants request reconsideration and withdrawal of the rejections made under 35 U.S.C. §112, second paragraph.

**VII. Rejection of Claims 24-25, 29-33, 41-42, and 45 under 35 U.S.C. §102(e) is Traversed, but Partly Accommodated**

The Examiner has maintained the rejection of claims 24-25, 29-33, 41-42, and 45 under 35 U.S.C. §102(e) as anticipated by Colpan et al. (U.S. Pat. 6,383,393; entire document). Applicants respectfully traverse this rejection.

The Patent Office alleges:

Colpan et al teaches methods for the purification of nucleic acids such as the isolation of plasmid of cosmid DNA from *E. coli* using an aqueous solution (column 2, line 1-10 and line 63-67). As demonstrated in examples 1, plasmid DNA is separated from the genomic DNA given A260/280 ratio and the large quantities of plasmid DNA, it is believed most of the plasmid DNA isolated from the genomic DNA. For the extraction of the DNA, the aqueous solution comprises high concentrations of chaotropic salts used in combination with aliphatic alcohols with a chain length of 1 to 5 carbon atoms (see e.g. column 4, line 66 through column 5, line 5). Specifically recited for use in the aqueous chaotropic solution is butanol (see e.g. column 5, line 20-27). Water is a weak base and is an essential element of the extraction mixture taught by Colpan et al. [P. 6.]

The Patent Office further alleges:

Applicants traverse the claim rejections under 35 U.S.C. 102 (e) and 103(a) on pages 19-21 of the amendment filed 1/26/05. Applicants argue that the present invention provides an extraction mixture, which can selectively extract plasmid DNA from total DNA with an organic solvent that is immiscible with the chaotropic-containing aqueous phase. Applicants state that the claims have been amended to emphasize this point. Applicants continue that in contrast to the instant invention, Colpan et al do not disclose a biphasic extraction mixture but disclose that the butanol is miscible with water within these ranges.

Applicants' arguments filed 1/26/05 have been fully considered but they are not persuasive. Colpan et al teach that within the range of 1 to 50%, butanol is miscible with water. Miscible is defined as combines with water but does not describe the completeness of this process. Therefore, it would be inherent that at some of the concentrations of butanol, some butanol will not enter the water and thus form an organic phase. This is schematically depicted in the figure on page 2 of the document labeled SCHP-445 and described in paragraph 2 of page 1. Three butyl alcohols are only partially soluble in water. [Pp. 7-8.]

Applicants respectfully disagree, but have amended claims 24-25 and 30-31. For example, claim 24 currently reads as follows:

24 (currently amended). A biphasic extraction mixture for selectively extracting plasmid DNA from genomic DNA in a DNA-containing material which comprises plasmid DNA and genomic DNA, in an extraction process, wherein the extraction mixture comprises butanol, a chaotrope, and water, wherein the butanol in the extraction mixture forms **an organic phase, which comprises plasmid DNA**, during the extraction process. [Emphasis added.]

Similar amendments have been made to claims 25, 30, and 31. Claims 29, 32, 33, 41, 42, and 45 are either directly or indirectly dependent on claim 24.

Colpan uses salts and alcohols to make the DNA less soluble so that it binds to a solid support. This solid support is an essential feature of the Colpan invention. Impurities are washed off the DNA while it is bound to the support and then “pure” DNA is eluted from the support. In contrast, the present invention uses butanol and water to partition and separate genomic DNA from plasmid DNA. Colpan will not work without a solid support to which the DNA becomes bound. The present invention does not use a solid support, and purification occurs while the DNA is entirely in solution.

The two processes are fundamentally different. Colpan does not teach that butanol can be used to partition plasmid DNA from genomic DNA, but actually teaches the opposite. For example:

The combination of chaotropic agents with high ionic strengths and hydrophobic organic..., alcohols...in the adsorption buffer ensure that in contrast to conventional purification methods the nucleic acids are **quantitatively fixed with high specificity on the surface of the mineral substrate**...[Col. 4; ll. 49-57; emphasis added.]



In the method of Colpan, the solubility of the DNA is decreased, so that it binds strongly to a solid matrix. Moreover, in Colpan, the butanol is only present in the “adsorption buffer,” because strictly speaking, the actual extraction buffer is used for eluting the DNA from the solid support and is a low salt buffer. Finally, in Colpan, the DNA is adsorbed out of solution onto a solid support, a clear contrast with the present invention.

For these reasons, Applicants respectfully traverse the rejection of claims 24-25, 29-33, 41-42, and 45 under 35 U.S.C. §102(e) and respectfully submit that the claims are in a condition for allowance.

Therefore, Applicants request reconsideration and withdrawal of the rejections made under 35 U.S.C. §102(e).

#### **VIII. Rejection of Claim 28 Under 35 U.S.C. §103(a) is Traversed**

The Examiner has maintained the rejection of claim 28 under 35 U.S.C. §103(a) as obvious over Colpan et al. (U.S. Pat. 6,383,393; entire document) in view of Sawadogo and Dyke (NAR, 19(3): 674 (1991); entire document). Applicants traverse this rejection.

The Patent Office alleges:

Applicants claim an extraction mixture, which comprises butanol, a chaotrope, and water. Butanol is n-butanol, 2-methylpropanol or butan-2-ol.

The teachings of Colpan et al are described above and are applied as before except; Colpan et al do not teach that Butanol is n-butanol, 2-methylpropanol or butan-2-ol.

Sawadogo and Dyke teach the use of n-butanol in the extraction of oligonucleotides (see e.g. column 1, paragraph 3).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the butanol taught by Colpan et al with the n-butanol taught by Sawadogo and Dyke because Colpan et al teach that it is within the ordinary skill of the art to use butanol in an extraction mixture and because Sawadogo and Dyke teach that it is within the ordinary skill of the art to

use n-butanol for extraction of DNA. One would have been motivated to do so in order to receive the expected benefit of reduced organic contaminants following use of n-butanol (Sawadogo and Dyke, page 674, column 1, paragraph 3). Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention. [P. 7.]

Other remarks by the Patent Office are outlined in the previous section.

Applicants arguments with respect to Colpan have also been outlined in the previous section and apply here as well. Moreover, Colpan teaches that the alcohol used in the adsorption process ensures that nucleic acids are quantitatively fixed to the solid matrix. One of skill in the art would therefore be encouraged to use alcohols that further enhance this adsorption process. In order to arrive at the claimed invention from Colpan, one of skill in the art would have to be encouraged to both substitute n-butanol, 2-methylpropanol, or butan-2-ol into the invention, dispense with the essential solid support, and analyze the organic phase for the presence of plasmid DNA. This motivation or encouragement is not provided by Sawadogo and Dyke.

In fact, Sawadogo and Dyke teaches that the organic phase formed by n-butanol is unsuitable for anything else but extracting contaminants from DNA:

The single H<sub>2</sub>O-containing n-butanol phase is removed and discarded. For some oligonucleotide preparations it may be necessary to repeat the n-butanol extraction to achieve complete removal of contaminants. [P. 674, col. 1.]

For these reasons, Applicants respectfully traverse the rejection of claim 28 under 35 U.S.C. §103(a) and respectfully submit that the claims are in a condition for allowance.

Therefore, Applicants request reconsideration and withdrawal of the rejections made under 35 U.S.C. §103(a).

**IX. Allowance of Claims 13, 14, 34, and 35 and Objection to Claims 43 and 44 are Acknowledged**

Applicants thank the Examiner for allowing claims 13, 14, 34, and 35 and respectfully request reconsideration of the remaining claims.

The Examiner has objected to claims 43 and 44 as being dependent upon a rejected base claim, but allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants thank the Examiner for this acknowledgement and have amended these claims accordingly. Applicants respectfully submit that claims 43 and 44 are in condition for allowance.

## X. Conclusion

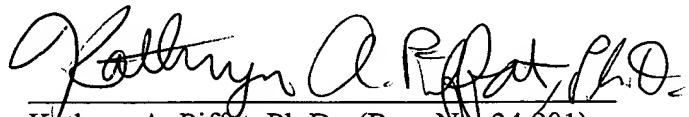
It is believed that all outstanding rejections have been addressed by this submission and that all the claims are in condition for allowance. If discussion of any amendment or remark made herein would advance this important case to allowance, the Examiner is invited to call the undersigned as soon as convenient.

In view of the foregoing amendments and remarks, the present application is respectfully considered in condition for allowance. An early reconsideration and notice of allowance are earnestly solicited.

Applicants believe that no extension of time is required. If, however, a petition for an extension of time is required, then the Examiner is requested to treat this as a conditional petition for an extension of time. Although it is not believed that any fee is required, in addition to any fee submitted herewith, to consider this submission, the Commissioner is hereby authorized to charge our deposit account no. 04-1105 should any fee be deemed necessary.

Respectfully submitted,

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